REMARKS

I. Status Summary

Claims 23-30 and 32-49 are pending in the present application and have been examined by the United States Patent and Trademark Office (hereinafter "the Patent Office"). Claims 23-25, 27-30, 32-34 and 37-49 currently stand rejected. Claims 26, 35 and 36 have been objected to.

Claims 27-30, 32, 43 and 48 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite.

Claims 27, 28, 30, 32, 43 and 47 have been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by Philip et al. (1998 *Cancer Gene Therapy* 5:236-246; hereinafter "Philip et al.").

Claims 27, 28, 30, 32, 43 and 48 have been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by U.S. Patent Application Publication No. 2002/0123479 to Song et al. (hereinafter "Song et al.").

Claims 27-30, 32, 43 and 47 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Philip et al. in view of PCT International Patent Application Publication No. WO 98/33527 to Cohen (hereinafter "Cohen") and PCT International Patent Application Publication No. WO 98/33527 to Warnier et al. (hereinafter "Warnier et al.").

Claims 23, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Song et al. in view of PCT International Patent Application No. WO96/04314 to Wong et al. (hereinafter "Wong et al.").

Claims 23, 25, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Song et al. and Wong et al. in view of PCT International Patent Application Publication No. WO 01/36680 to Eastman et al. (hereinafter "Eastman et al.") and PCT International Patent Application Publication No. WO 02/36790 to Schuller et al. (hereinafter "Schuller et al.").

Claims 23, 24, 27, 28, 29, 30, 32-34 and 37-49 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Song et al. and Wong et al. in view of Cohen et al. and Warnier et al.

Claims 26, 35 and 36 have been objected to upon the contention that they are based upon rejected base claims.

Claims 26, 27, 35 and 48 have been amended herein. Support for the amendments can be found throughout the specification as originally filed, and particularly in original claims 23, 26, 27, 33, and 35; and at page 6 through page 7 of the specification. No new matter has been added.

Reconsideration of the application in view of the amendments and remarks set forth herein is respectfully requested.

II. Responses to the Rejection Under 35 U.S.C. § 112, second paragraph

Claims 27-30, 32, 43 and 48 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite. The Patent Office contends that claim 27 recites "the patient" which allegedly lacks proper antecedent basis. Furthermore, the Patent Office contends that claim 48 recites "the method according to claim 27", which is allegedly improper since claim 27 is a product claim.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Without acquiescing to the contentions of the Patent Office applicants respectfully submit that claim 27 has been amended to clarify the claimed subject matter. In particular, claim 27 has been amended to recite, *inter alia*, "A pharmaceutical composition comprising antigen-presenting cells...wherein the antigen-presenting cells are semi-allogeneic and HLA-haploidentical with respect to those of [[the]] a patient with a tumor disease, wherein HLA-haploidentical antigen-presenting cells have class I and class II molecules in common with the patient, and wherein said proteins and/or peptides are overexpressed in tumor cells of [[a]] the patient with a tumor disease or are derived from tumor cells from the patient." Support for the amendments can be found

throughout the specification as originally filed, and particularly in original claim 27 and at page 6 through page 7 of the specification. No new matter has been added.

Without acquiescing to the contentions of the Patent Office applicants respectfully submit that claim 48 has been amended by replacing "method" with "pharmaceutical composition". Support for the amendments can be found throughout the specification as originally filed, and particularly in original claim 27. No new matter has been added.

Applicants respectfully submit that present claims 27 and 48 are believed to be in compliance with 35 U.S.C. § 112, second paragraph. Since claims 28-30, 32 and 43 depend directly or indirectly from claim 27 they too are believed to be in compliance with 35 U.S.C. § 112, second paragraph. As such, applicants respectfully request that the instant rejection be withdrawn. A Notice of Allowance is also respectfully requested.

III. Responses to the Rejection Under 35 U.S.C. § 102(b) Over Philip et al.

Claims 27, 28, 30, 32, 43 and 47 have been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by Philip et al. (1998 *Cancer Gene Therapy* 5:236-246; hereinafter "Philip et al."). The Patent Office contends that Philip et al. disclosed the expression of MART-1 cDNA in human dendritic cells prepared from healthy individuals as well as peptide-loaded dendritic cells. The Patent Office contends that the dendritic cells in Philip et al. are inherently haploidentical to an appropriate recipient and possess an HLA-haplotype 50% identical to an appropriate recipient. As such, the Patent Office contends that Philip et al. teaches each and every element of the rejected claims.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Applicants preliminarily note it is well settled that for a cited reference to qualify as prior art under 35 U.S.C. §102, each element of the claimed subject matter must be disclosed within the reference. "A claim is anticipated only if each and every element in the claim is found, either expressly or inherently described, in a single prior art

reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Claim 27 is directed to a pharmaceutical composition comprising, *inter alia*, antigen-presenting cells, wherein the antigen-presenting cells are semi-allogeneic and HLA-haploidentical with respect to those of a patient, wherein HLA-haploidentical antigen-presenting cells have class I and class II molecules in common with the patient. Applicants respectfully submit that Philip et al. fails to disclose antigen-presenting cells that are semi-allogeneic and HLA-haploidentical with respect to those of a patient, and wherein the HLA-haploidentical antigen-presenting cells have class I and class II molecules in common with the patient. Indeed, there appears to be no mention or consideration of HLA haplotype of the dendritic cells in Philip et al. As such, applicants respectfully submit that Philip et al. fails to provide for each and every element of claim 27 and therefore fails to support a rejection of claim 27 under 35 U.S.C. § 102(b).

The Patent Office contends that the dendritic cells in Philip et al. are inherently haploidentical to an appropriate recipient and possess an HLA-haplotype 50% identical to an appropriate recipient. Applicants respectfully disagree. Applicants respectfully submit that the Patent Office has failed to present a *prima facie* case of inherency. In particular, applicants respectfully submit that MPEP § 2112 recites, *inter alia*:

> The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

(emphasis added).

The Patent Office suggests that the dendritic cells of Philip et al. are inherently haploidentical to an appropriate recipient. Applicants respectfully submit that the Patent Office's use of the term "appropriate recipient" shows that the dendritic cells of Philip et al. are not inherently haploidentical. For them to be inherently haploidentical they would have to always be haploidentical regardless of who the patient would be. In determining inherency, the Patent Office may not point to certain results or characteristics that may occur. Here it appears the Patent Office simply alleges that the dendritic cells used by Philip et al. may be haploidentical to some patients but that does not mean they are necessarily haploidentical as required by MPEP § 2112.

Moreover, even if the dendritic cells of Philip et al. are HLA matched to an appropriate recipient, they are not haploidentical as the term is used in the presently disclosed and claimed subject matter. Applicants respectfully submit that the instant rejection appears to be premised, at least in part, on the Patent Office's incorrect understanding of "haploidentical". The use of "haplo" derives from *haploid* which represents the genetic constellation in the egg or the sperm which is combined in the *diploid* zygote to form a new individual. HLA-haploidentical is correctly referred to as sharing of an HLA haplotype (i.e. the HLA region on chromosome 6, which includes three MHC class I alleles and 3 MHC class II alleles). In haploidentical individuals, cells, APCs, etc. the shared HLA haplotype is identical by genetic descent, i.e. the individuals, cells, APCs, etc. are genetically related. That is, the shared HLA-haplotypes are haploidentical because they are genetically identical by descent from the same parent. Importantly, because the chromosomes are passed on to the next generation through the sperm and the egg, the entire genetic information of all 3 HLA class I alleles and all 3 HLA class II alleles will be genotypically identical on shared HLA haplotypes, i.e. HLA-haploidentical.

There is great diversity in the HLA genetic system, which is the most polymorphic genetic system in man. Therefore when cells or APCs are derived from two unrelated individuals they are referred to as allogeneic. If cells or APCs are derived from the same individual they are referred to as syngeneic. By genetic typing it is possible to identify unrelated individuals who are partially or fully matched for HLA alleles. These

two individuals are referred to as HLA-matched in the case of genetically identical sequences or HLA-mismatched, in the case of genetically different sequences for any of the HLA class I or class II alleles. Even if there is a full HLA match for all HLA class I and class II alleles, these individuals are referred to as fully HLA-matched but not as HLA-haploidentical because they are not genetically identical by descent. If there are only partial matches, the cells may be referred to as "semi-allogeneic". The term "semi-allogeneic" may be used for cells of unrelated individuals that share some MHC class I or class II alleles and differ by some class I or class II alleles. Since this is also the case in cells or APCs that are HLA-haploidentical they too may be referred to as semi-allogeneic. However, this is a one-way usage. HLA-haploidentical can be designated as semi-allogeneic but semi-allogeneic does not imply HLA-haploidentical, because semi-allogeneic does not strictly mean identity of one HLA-haplotype by genetic descent.

The last full paragraph of page 7 of the specification of the present application states as follows:

> HLA-haploidentical antigen-presenting cells have class I (HLA-A, -B, and -C) molecules in common with the patient which are encoded by the HLA-A, -B, and-C alleles of one chromosome. They also have class II molecules (HLA-DR, -DQ, and DP) in common with the patient encoded by the corresponding alleles of the same chromosome.

(emphasis added). Accordingly, the HLA-haploidentical antigen-presenting cells of the presently disclosed and claimed subject matter have each of the class I molecules HLA-A, -B, and -C and each of the class II molecules HLA-DR, -DQ, and -DP that are encoded by the corresponding alleles of a chromosome in common with those of the patient.

Philip et al. does not describe that the HLA alleles are genetically identical by descent. Furthermore, Philip et al. does not describe that all 3 HLA class I alleles and all 3 HLA class II alleles are genotypically identical on shared HLA haplotypes, i.e. HLA-haploidentical, as presently claimed. Philip et al., at best, suggests that it is desirable to express complete TAA proteins in dendritic cells to allow the dendritic cells to process and present both class I- and class II-restricted epitopes. Philip et al. is silent on

haploidentical cells and the 3 HLA class I and the 3 HLA class II alleles. As such, applicants respectfully submit that the disclosure of Philip et al. is not believed to inherently provide dendritic cells that are haploidentical to a subject as presently claimed.

Taken together, applicants respectfully submit that Philip et al. fails to provide for each and every element of claim 27. In particular, Philip et al. fails to disclose or inherently provide antigen-presenting cells that are semi-allogeneic and HLA-haploidentical with respect to those of a patient, and have class I and class II molecules in common with the patient, as presently claimed. As such, applicants respectfully submit that Philip et al. fails to support a rejection of claim 27 under 35 U.S.C. § 102(b). Since claims 28, 30, 32, 43 and 47 depend either directly or indirectly from claim 27 they too are believed to be distinguished from Philip et al.

Accordingly, applicants respectfully submit that the rejection of claims 27, 28, 30, 32, 43 and 47 under 35 U.S.C. § 102(b) has been addressed. As such, applicants respectfully request that the instant rejection be withdrawn at this time, and further respectfully solicit a Notice of Allowance of claims 27, 28, 30, 32, 43 and 47.

IV. Responses to the Rejection Under 35 U.S.C. § 102(b) Over Song et al.

Claims 27, 28, 30, 32, 43 and 48 have been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by U.S. Patent Application Publication No. 2002/0123479 to Song et al. (hereinafter "Song et al."). The Patent Office contends that Song et al. disclosed dendritic cells comprising an expression vector which direct expression of antigens associated with cancers. Moreover, the Patent Office contends that Song et al. disclosed a method of treatment of cancer comprising administration of a dendritic cell population transduced *ex vivo*. Finally, the Patent Office contends that the *ex vivo* transduced dendritic cells of Song et al. are allegedly inherently haploidentical.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Applicants preliminarily note it is well settled that for a cited reference to qualify as prior art under 35 U.S.C. §102, each element of the claimed subject matter must be disclosed within the reference. "A claim is anticipated only if each and every element in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Claim 27 is directed to a pharmaceutical composition comprising, *inter alia*, antigen-presenting cells, wherein the antigen-presenting cells are semi-allogeneic and HLA-haploidentical with respect to those of a patient, wherein HLA-haploidentical antigen-presenting cells have class I and class II molecules in common with the patient. Applicants respectfully submit that Song et al. fails to disclose antigen-presenting cells that are semi-allogeneic and HLA-haploidentical with respect to those of a patient, and wherein the HLA-haploidentical antigen-presenting cells have class I and class II molecules in common with the patient. Song et al., at best, appears to only make a singular mention of haplotype in paragraph [0184]. Even then, Song et al. does not indicate what haplotype is being considered and fails to mention HLA haplotype. Applicants respectfully note that haplotype can refer to a member of any chromosome pair. As such, applicants respectfully submit that Song et al. fails to provide for each and every element of claim 27 and therefore fails to support a rejection of claim 27 under 35 U.S.C. § 102(b).

The Patent Office contends that the dendritic cells in Song et al. are inherently haploidentical to an appropriate recipient and possess an HLA-haplotype 50% identical to an appropriate recipient. Applicants respectfully disagree. Applicants respectfully submit that the Patent Office has failed to present a *prima facie* case of inherency, and direct the Patent Office's attention to MPEP § 2112 as set forth hereinabove.

The Patent Office suggests that the dendritic cells of Song et al. are inherently haploidentical to an appropriate recipient. Applicants respectfully submit that the Patent Office's use of the term "appropriate recipient" shows that the dendritic cells of Song et al. are not inherently haploidentical. For them to be inherently haploidentical they would have to always be haploidentical regardless of who the patient would be. In determining

inherency, the Patent Office may not point to certain results or characteristics that may occur. Here it appears the Patent Office simply alleges that the dendritic cells used by Song et al. may be haploidentical to some patients but that does not mean they are necessarily haploidentical as required by MPEP § 2112.

Moreover, even if the dendritic cells of Song et al. are HLA matched to an appropriate recipient, they are not haploidentical as the term is used in the presently disclosed and claimed subject matter. Applicants respectfully submit that the instant rejection appears to be premised, at least in part, on the Patent Office's incorrect understanding of "haploidentical". Applicants respectfully direct the Patent Office's attention to the discussion of haploidentical hereinabove.

Song et al. does not describe that the HLA alleles are genetically identical by descent. Furthermore, Song et al. does not describe that all 3 HLA class I alleles and all 3 HLA class II alleles are genotypically identical on shared HLA haplotypes, i.e. HLA-haploidentical, as presently claimed. Song et al. is silent with regard to haploidentical cells and the 3 HLA class I and the 3 HLA class II alleles. As such, applicants respectfully submit that the disclosure of Song et al. is not believed to inherently provide dendritic cells that are haploidentical to a subject as presently claimed.

Taken together, applicants respectfully submit that Song et al. fails to provide for each and every element of claim 27. In particular, Song et al. fails to disclose or inherently provide antigen-presenting cells that are semi-allogeneic and HLA-haploidentical with respect to those of a patient, and have class I and class II molecules in common with the patient, as presently claimed. As such, applicants respectfully submit that Song et al. fails to support a rejection of claim 27 under 35 U.S.C. § 102(b). Since claims 28, 30, 32, 43 and 48 depend either directly or indirectly from claim 27 they too are believed to be distinguished from Song et al.

Accordingly, applicants respectfully submit that the rejection of claims 27, 28, 30, 32, 43 and 48 under 35 U.S.C. § 102(b) has been addressed. As such, applicants respectfully request that the instant rejection be withdrawn at this time, and further respectfully solicit a Notice of Allowance of claims 27, 28, 30, 32, 43 and 48.

V. Responses to the Obviousness Rejections

Claims 27-30, 32, 43 and 47 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Philip et al. in view of Cohen et al. and Warnier et al. Claims 23, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Song et al. in view of PCT International Patent Application No. WO96/04314 to Wong et al. (hereinafter "Wong et al."). Claims 23, 25, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Song et al. and Wong et al. in view of Eastman et al. and Schuller et al. Claims 23, 24, 27, 28, 29, 30, 32-34 and 37-49 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Song et al. and Wong et al. in view of Cohen et al. and Warnier et al.

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejection and submit the following remarks.

V.A. Response to the Rejection over Philip et al. in view of Cohen et al. and Warnier et al.

Claims 27-30, 32, 43 and 47 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Philip et al. in view of Cohen et al. and Warnier et al. The Patent Office contends that Philip et al. teaches each and every element of the rejected claims except the incorporation of DNA or RNA encoding for at least one tumor antigen introduced into an antigen presenting cell. However, the Patent Office contends that Cohen et al. and Warnier et al. compensate for this deficiency. As such, the Patent Office contends that it would have been *prima facie* obvious at the time the claimed invention was made to pulse or transduce the dendritic cells of Philip et al. using peptides or cDNA from more than one tumor cell line based on the alleged disclosure of Cohen et al. and Warnier et al.

Applicants respectfully submit that the deficiencies in the disclosure of Philip et al. with regard to the presently disclosed and claimed subject matter, as noted hereinabove in the discussion of the rejection under 35 U.S.C. 102(b), are believed to be equally applicable to the instant rejection. Applicants respectfully submit that neither

Cohen et al. nor Warnier et al., nor the combination thereof, are believed to compensate for these deficiencies. In particular, applicants respectfully submit that neither Cohen et al. nor Warnier et al. provide antigen-presenting cells that are semi-allogeneic and HLA-haploidentical, as presently claimed. As discussed in Amendment G filed on October 7, 2009, Cohen et al., at best, describes the use of semi-allogeneic cells, rather than HLA-haploidentical cells, and fails to teach or disclose that all of the alleles encoding both the class I molecules HLA-A, -B, and -C and the class II molecules HLA-DR, -DQ, and -DP on the same chromosome are matched. There is believed to be no disclosure in Warnier et al. that teaches or suggests the use of HLA-haploidentical APCs as presently claimed. As such, the proposed combination of Philip et al., Cohen et al. and Warnier et al. fails to provide for each and every element of the currently rejected claims. As such, applicants respectfully submit that even assuming *arguendo* that one of ordinary skill in the art would be motivated to combine the references as proposed by the Patent Office, the proposed combination fails to teach or suggest each and every element of the instant claims. Thus, the proposed combination of Philip et al., Cohen et al. and Warnier et al. is not believed to render obvious the presently claimed subject matter and therefore fails to support a rejection of the instant claims under 35 U.S.C. § 103(a).

Furthermore, the Patent Office alleges that the phrase "at least one" in Cohen et al. is suggestive for using multiple tumor antigens. However, Cohen et al. is not believed to teach an embodiment where more than one tumor antigen is utilized. As such, applicants respectfully submit that claim 29 is believed to be further distinguished from the proposed combination of Philip et al., Cohen et al. and Warnier et al.

Taken together, applicants respectfully submit that the Patent Office has failed to present a *prima facie* case of obviousness. Applicants respectfully submit that the proposed combination of Philip et al., Cohen et al. and Warnier et al. fails to support the instant rejection of claim 27 under 35 U.S.C. § 103(a). Since claims 28-30, 32, 43 and 47 depend from claim 27 they too are believed to be distinguished from the proposed combination. Thus, applicants respectfully request that the instant rejection be withdrawn at this time. A Notice of Allowance is also respectfully requested.

V.B. Response to the Rejection over Song et al. and Wong et al.

Claims 23, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Song et al. in view of Wong et al. The Patent Office contends that Song et al. teaches each and every element of the rejected claims except that haplotype-matched transduced dendritic cells are administered for the treatment of cancer in a subject. However, the Patent Office contends that Wong et al. compensates for this deficiency by allegedly teaching that host-compatible antigen-presenting cells into which recombinant DNA is introduced may be administered to a subject. As such, the Patent Office contends that it would have been *prima facie* obvious at the time that the claimed invention was made to administer the haplotype-matched dendritic cells of Song et al. for the treatment of cancer in a subject in view of the disclosure of Wong et al.

Applicants respectfully submit that the deficiencies in the disclosure of Song et al. with regard to the presently disclosed and claimed subject matter, as noted hereinabove in the discussion of the rejection under 35 U.S.C. 102(b), are believed to be equally applicable to the instant rejection. Applicants respectfully submit that Wong et al. fails to compensate for these deficiencies. In particular, applicants respectfully submit that Wong et al. fails to provide antigen-presenting cells that are semi-allogeneic and HLA-haploidentical, as presently claimed. The Patent Office contends that Wong et al. teach "host compatible" antigen presenting cells, which allegedly means APCs that are of the same haplotype of the subject or "host" to which the cells are administered. However, applicants respectfully submit that indicating that APCs are of the same haplotype of the subject to which the cells are administered is not equivalent to providing APCs that are semi-allogeneic and HLA-haploidentical, as presently claimed. Applicants respectfully direct the Patent Office's attention to the discussion hereinabove regarding the meaning of semi-allogeneic and HLA-haploidentical. Wong et al. is not believed to describe that the HLA alleles are genetically identical by descent. Furthermore, Wong et al. is not believed to describe that all 3 HLA class I alleles and all 3 HLA class II alleles are genotypically identical on shared HLA haplotypes, i.e. HLA-haploidentical, as presently claimed. Wong et al. is silent with regard to haploidentical cells and the 3 HLA class I

and the 3 HLA class II alleles. As such, applicants respectfully submit that the disclosure of Wong et al. is not believed to provide APCs that are haploidentical to a subject as presently claimed.

As such, applicants respectfully submit that even assuming *arguendo* that one of ordinary skill in the art would be motivated to combine the references as proposed by the Patent Office, the proposed combination fails to teach or suggest each and every element of the instant claims. Thus, the proposed combination of Song et al. and Wong et al. is not believed to render obvious the instant subject matter and therefore fails to support a rejection of the instant claims under 35 U.S.C. § 103(a).

Continuing with the instant rejection, applicants respectfully submit that one of ordinary skill in the art would not have been motivated to combine the references as proposed by the Patent Office to arrive at the presently disclosed and claimed subject matter, and indeed would be dissuaded from doing so. The Patent Office refers to paragraph [0184] of Song et al. in contending that *ex vivo* transduced monocytes/macrophages and dendritic cells are excellent sources for transferring immune responses. However, applicants respectfully submit that in the same paragraph, Song et al. states that "due to logistical and other complications associated with *ex vivo* gene therapy, directly administering gene delivery vehicles to a patient is preferred. In particularly preferred approaches, *in vivo* transduction of dendritic cells is performed." Indeed, Song et al. is directed to genetically modifying dendritic cells either *in vivo* or *ex vivo* (*see*, e.g., the Abstract), and based on their data in the Examples indicates that the *in vivo* approach is superior. As such, one of ordinary skill in the art, upon reviewing Song et al. in its entirety, would be dissuaded from employing the *ex vivo* approach and would instead be motivated to modify dendritic cells *in vivo*. Thus, Song et al. appears to teach away from the presently disclosed and claimed subject matter, and would therefore dissuade one of ordinary skill in the art from employing the teachings of Song et al., alone or in combination with Wong et al., to arrive at the presently claimed subject matter.

Moreover, Wong et al. is, at best, directed to MHC fusion complexes to be directly administered to a subject. Out of the 147 page document, Wong et al. only briefly mentions the possibility of employing APCs as a means of introducing the fusion complexes to a subject. *See*, e.g. page 35, line 8, through page 36, line 10 of Wong et al. As such, one of ordinary skill in the art, upon reviewing Song et al. and Wong et al. in their entireties, would not have been motivated to combine the references to arrive at a method for the generation of HLA-haploidentical antigen presenting cells, as recited in claim 23, or a pharmaceutical composition comprising antigen-presenting cells, as recited in claim 27. As such, it appears that the Patent Office is impermissibly relying upon hindsight in making the proposed combination.

Taken together, applicants respectfully submit that the Patent Office has failed to present a *prima facie* case of obviousness. Applicants respectfully submit that the proposed combination of Song et al. and Wong et al. fails to support the instant rejection of claims 23 and 27 under 35 U.S.C. § 103(a). Since claims 28, 30, 32-34, 37-40, 43-45 and 47-49 depend from claims 23 and 27 they too are believed to be distinguished from the proposed combination. Thus, applicants respectfully request that the instant rejection be withdrawn at this time. A Notice of Allowance is also respectfully requested.

V.C. Response to the Rejection over Song et al. and Wong et al. in view of Eastman et al. and Schuller et al.

Claims 23, 25, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Song et al. and Wong et al. in view of Eastman et al. and Schuller et al. The Patent Office contends that Song et al. and Wong et al. provide for each and every element of the claims except the reverse transcription of amplified cDNA into RNA. However, the Patent Office contends that Eastman et al. and Schuller et al. compensate for these deficiencies. Applicants respectfully disagree.

Applicants respectfully submit that the deficiencies in the proposed combination of Song et al. and Wong et al. with regard to the presently disclosed and claimed subject matter, as noted hereinabove, are believed to be equally applicable to the

instant rejection. Applicants respectfully submit that Eastman et al. and Schuller et al. fail to cure these deficiencies. For example, applicants respectfully submit that there is believed to be no disclosure in either Eastman et al. or Schuller et al. that teaches or suggests the use of HLA-haploidentical APCs as presently claimed. As such, applicants respectfully submit that even assuming *arguendo* that one of ordinary skill in the art would be motivated to combine the references as proposed by the Patent Office, the proposed combination fails to teach or suggest each and every element of the instant claims. Moreover, Eastman et al. and Schuller et al. are not believed to overcome the lack of motivation to combine or teaching away from the presently disclosed and claimed subject matter noted above. Thus, the combination does not render obvious the instant subject matter and therefore fails to support a rejection of the instant claims under 35 U.S.C. § 103(a).

Accordingly, applicants respectfully submit that the instant obviousness rejection of claims 23, 25, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 over Song et al. and Wong et al. in view of Eastman et al. and Schuller et al. has been addressed, and respectfully request that it be withdrawn at this time. Applicants further respectfully submit that claims 23, 25, 27, 28, 30, 32-34, 37-40, 43-45 and 47-49 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

V.D. Response to the Rejection over Song et al. and Wong et al. in view of Cohen et al. and Warnier et al.

Claims 23, 24, 27, 28, 29, 30, 32-34 and 37-49 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Song et al. and Wong et al. in view of Cohen et al. and Warnier et al. It appears that the Patent Office relies upon Cohen et al. and Warnier et al. for the disclosure of the use of polynucleotides or polypeptides from several different tumor cell lines. As such, the Patent Office contends that it would have been *prima facie* obvious at the time that the claimed invention was made to combine Song et al. and Wong et al. with Cohen et al. and Warnier et al. to arrive at the subject matter of the currently rejected claims. Applicants respectfully disagree.

Applicants respectfully submit that the deficiencies in the proposed combination of Song et al. and Wong et al. with regard to the presently disclosed and claimed subject matter, as noted hereinabove, are believed to be equally applicable to the instant rejection. Applicants respectfully submit that Cohen et al. and Warnier et al. fail to cure these deficiencies. For example, applicants respectfully submit that there is believed to be no disclosure in either Cohen et al. and Warnier et al. that teaches or suggests the use of HLA-haploidentical APCs as presently claimed. As such, applicants respectfully submit that even assuming *arguendo* that one of ordinary skill in the art would be motivated to combine the references as proposed by the Patent Office, the proposed combination fails to teach or suggest each and every element of the instant claims. Moreover, Cohen et al. and Warnier et al. are not believed to overcome the lack of motivation to combine or teaching away from the presently disclosed and claimed subject matter noted above. Thus, the combination does not render obvious the instant subject matter and therefore fails to support a rejection of the instant claims under 35 U.S.C. § 103(a).

Accordingly, applicants respectfully submit that the instant obviousness rejection of claims 23, 24, 27, 28, 29, 30, 32-34 and 37-49 over Song et al. and Wong et al. in view of Cohen et al. and Warnier et al. has been addressed, and respectfully request that it be withdrawn at this time. Applicants further respectfully submit that claims 23, 24, 27, 28, 29, 30, 32-34 and 37-49 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

VI. Responses to the Claim Objections

Claims 26, 35 and 36 have been objected to upon the contention that they are based upon rejected base claims.

Without acquiescing to the contentions of the Patent Office and in an effort to advance prosecution, applicants respectfully submit that claims 26 and 35 have been amended to independent format. Claim 36 now depends from independent claim 35. As such, applicants respectfully submit that the instant objection with regard to claims

26, 35 and 36 has been addressed. Claims 26, 35 and 36 are believed to be in condition for allowance. A Notice of Allowance is therefore respectfully requested.

CONCLUSION

In light of the above, it is respectfully submitted that the present application is now in proper condition for allowance, and a Notice of Allowance to that effect is earnestly solicited.

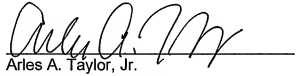
If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,
JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: 06/17/2010

By: 

Arles A. Taylor, Jr.
Registration No. 39,395
Customer No. 25297
(919) 493-8000

1406/468 AAT/LRL/dbp